The Family History Method: Whose Psychiatric History Is Measured?

Kenneth S. Kendler, M.D., Judy L. Silberg, Ph.D., Michael C. Neale, Ph.D., Ronald C. Kessler, Ph.D., Andrew C. Heath, D.Phil., and Lindon J. Eaves, Ph.D., D.Sc.

Objective: The family history method, in which an informant is asked about the history of psychiatric illness in relatives, is widely used in psychiatric research. Previous research has examined the influence on family history information of characteristics of the relative. In this report, the authors seek to clarify the impact on family history reporting of the psychiatric history of the informant. Method: Both members of female twin pairs from a population-based twin registry were asked about the history of major depression, generalized anxiety disorder, and alcoholism in their mother and father. The authors examined twin pairs discordant for each of the three diagnoses and predicted that the affected twin would report higher rates of the same disorder in her parent than would the unaffected twin. Results: Twins with a history of major depression or generalized anxiety disorder but not twins with alcoholism were significantly more likely to report the same disorder in their parents than were their unaffected co-twins. Conclusions: For major depression and generalized anxiety disorder, a family history diagnosis appears to reflect the psychiatric history of both the relative and the informant. Caution may be needed in the interpretation of results based on the family history method, although the magnitude of this problem may be attenuated by the use of multiple informants.


Knowledge of the psychopathological status of the relatives of psychiatric patients is important in many aspects of psychiatric research and practice. Because assessing relatives directly is time-consuming, inconvenient, and often expensive, it is common practice to ask the patient or a cooperative relative about the presence of psychiatric disorders in other relatives. This technique, called the “family history method,” is distinguished from direct evaluation of individual relatives, termed the “family study method.”

The family history method has been extensively evaluated, especially in the assessment of major depression, and results have consistently demonstrated relatively high specificity but low-to-moderate sensitivity (1–6). Further investigations have examined characteristics of the relative (the individual about whom questions are being asked) that affect the sensitivity of family history information. The sensitivity of the family history method increases if the relative has received treatment (especially hospitalization), has a severe psychiatric disorder or severe symptoms, or is a spouse or parent (3, 6, 7). Less attention has been devoted to examining characteristics of the informant (the individual giving information about his or her relatives) that influence family history information. The sole informant characteristic examined to date has been the relationship with the relative. The results of such studies have been inconsistent. For example, Thompson et al. (3) found that spouses and offspring provided more accurate family history information than parents or siblings, but Andreassen et al. (1) found parents to be better informants than siblings or offspring.

In this report, we examine the impact on family history information of the psychiatric history of the informant. We hypothesized that informants who have suffered from a psychiatric disorder would be more likely than informants with no psychiatric history to report the presence of that disorder in relatives.
METHOD

Sample

The subjects of this study were Caucasian female same-sex twins from the population-based Virginia Twin Register, formed from a systematic review of all birth records in the Commonwealth of Virginia. Twins were eligible to participate in this study if both members of the pair had previously responded to a mailed questionnaire, to which the individual response rate was 64%. We succeeded in personally interviewing 2,163 (92.0%) of the 2,352 individuals from 1,176 twin pairs who met these criteria. The 2,163 individuals included both members of 1,033 pairs and one member of 97 pairs. Of the completed interviews, 1,932 (89.3%) were performed face to face and 231 (10.7%) were conducted by telephone. The mean ± SD age of the sample at interview was 30.1 ± 7.6 years and ranged from 17 to 55.

Measures, Interviewers, and Diagnostic Review

The diagnoses of major depression, generalized anxiety disorder, and alcohol dependence in the twins were made by using an adaptation of the Structured Clinical Interview for DSM-III-R (8). Each twin was also asked about a history of major depression, generalized anxiety disorder, and alcoholism in her mother and father. Family History Research Diagnostic Criteria (FH-RDC) (9) were used for major depression and alcoholism. Since no FH-RDC existed for generalized anxiety disorder, we created our own, requiring a period of at least 1 month, which was not part of an obvious justified stress reaction, in which the relative was particularly tense, anxious, or worried and either received treatment for these feelings or had three or more of the following symptoms: 1) being keyed up or on edge, 2) irritability, 3) restlessness, 4) having trouble falling asleep, or 5) tiring easily.

All interviewers underwent extensive and ongoing training during the field study, and each had a minimum of a master’s degree in psychology or social work or a bachelor’s degree plus at least 2 years of clinical experience. The same interviewer never interviewed both members of a twin pair.

The diagnoses of major depression, generalized anxiety disorder, and alcohol dependence (hereafter termed “alcoholism”) in the twins were based on a blind review by one of us (K.S.K.), an experienced psychiatric diagnostician, using DSM-III-R criteria with one modification. In order to have a sufficient sample size of twin pairs discordant for generalized anxiety disorder, it was necessary to lower the minimum duration from 6 months, as specified in DSM-III-R, to 1 month, as specified in DSM-III. The family history diagnoses were assigned by a computer algorithm operationalizing the previously specified criteria.

Interrater reliability was assessed in 53 jointly conducted interviews. Each of these interviews was blindly reviewed; the chance corrected agreement (kappa) (10) for the diagnoses of major depression and generalized anxiety disorder, as defined above, were 0.96 ± 0.04 and 0.77 ± 0.10, respectively. No cases of alcoholism occurred in the 53 jointly interviewed twins. The kappa value for the family history diagnoses was unity for depression and generalized anxiety disorder in the father and depression and alcoholism in the mother; for alcoholism in the father and generalized anxiety disorder in the mother the kappa values were 0.93 ± 0.06 and 0.95 ± 0.05, respectively.

Statistical Analysis

To explore the impact on family history information of an informant’s psychiatric history, three conditions should be met. 1) The relatives assessed by the family history method should be matched or, more ideally, should be the same individuals. 2) The informants should be matched for family background so that differences in rates of illness reported in relatives do not reflect differences in familial liability to illness. 3) The informants should differ in their psychiatric history. All three of these conditions are met in our design, in which we compare the family history reports regarding parents from members of twin pairs discordant for the psychiatric disorder of interest. The significance of the association between the psychiatric history of the informant and that assigned to the parent was assessed by using McNemar’s chi-square test with one degree of freedom (11). Reported p values are two-tailed.

RESULTS

As seen in table 1, our hypothesis that an informant with a particular disorder would be more likely to report that disorder in a relative was strongly confirmed for major depression and generalized anxiety disorder. For example, we found 334 twin pairs in our sample who were discordant for a lifetime diagnosis of major depression and who both provided family history information on their mother. In 181 of these pairs, both twins agreed that their mother had never had an episode of depression, and in 58 both twins agreed that their mother had been depressed. In 115 pairs, the twins disagreed about the diagnosis of depression in their mother. These 115 pairs were divisible into two groups: 1) the unaffected twin reported illness in the mother and the affected twin did not and 2) the affected twin reported illness in their mother and the unaffected twin did not. If an informant’s psychiatric history does not influence reporting of family history information, these two groups should be approximately equal in size. However, the latter group (N=79) was more than twice as large as the former group (N=36), a distribution that would very rarely occur by chance (table 1).

A similar pattern of results was found for generalized anxiety disorder in the mother and father. For major
TABLE 1. Family History Diagnoses in Parents Reported by Twins Discordant for Psychiatric Illness

<table>
<thead>
<tr>
<th>Lifetime Diagnosis of Twin</th>
<th>Parent</th>
<th>Number of Pairs*</th>
<th>By Neither Twin</th>
<th>By Unaffected Twin Only</th>
<th>By Affected Twin Only</th>
<th>By Both Twins</th>
<th>( \chi^2 ) (df=1)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major depression</td>
<td>Mother</td>
<td>354</td>
<td>181</td>
<td>36</td>
<td>79</td>
<td>58</td>
<td>15.34</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>Father</td>
<td>349</td>
<td>258</td>
<td>26</td>
<td>41</td>
<td>24</td>
<td>2.92</td>
<td>0.09</td>
</tr>
<tr>
<td>Generalized anxiety disorder</td>
<td>Mother</td>
<td>316</td>
<td>168</td>
<td>31</td>
<td>77</td>
<td>40</td>
<td>18.75</td>
<td>0.00001</td>
</tr>
<tr>
<td></td>
<td>Father</td>
<td>306</td>
<td>214</td>
<td>22</td>
<td>55</td>
<td>15</td>
<td>13.30</td>
<td>0.0002</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>Mother</td>
<td>86</td>
<td>70</td>
<td>2</td>
<td>4</td>
<td>10</td>
<td>0.17</td>
<td>0.68</td>
</tr>
<tr>
<td></td>
<td>Father</td>
<td>85</td>
<td>52</td>
<td>4</td>
<td>8</td>
<td>21</td>
<td>0.75</td>
<td>0.39</td>
</tr>
</tbody>
</table>

* Number of twin pairs discordant for a given lifetime diagnosis, where both twins provided a family history diagnosis of given parent.

depression in the father, the results were similar but far less statistically robust. For alcoholism, where the sample size of discordant twin pairs was much smaller, the results, although in the same direction, fell far short of statistical significance.

DISCUSSION

Our results suggest that for major depression and generalized anxiety disorder, family history information is substantially influenced by the psychiatric history of the informant. Informants with a personal history of major depression or generalized anxiety disorder were considerably more likely to report the same syndrome in a relative than were informants without such a history. The results for alcoholism are more ambiguous. Although our results showed no significant evidence for a similar effect, the size of our sample of discordant pairs was too small to provide a powerful test.

Our findings are explicable as part of a general cognitive mode in which the reporting of perceptions are influenced by experiences and expectations. Other studies have shown that reports on relatives for such variables as educational attainment (12), body silhouette (13), social attitudes (14), and temperament (15) are influenced by similar characteristics in the informant. In particular, our results are consistent with work in progress showing that a twin's rating of her own history of depressive symptoms influences her rating of the history of depressive symptoms in her co-twin (16).

The present results do not address the specific processes by which this pattern emerges, however. It could derive from differences in the propensity to recognize psychopathology in a relative. Personal experience of a psychiatric illness may alter an individual's ability to perceive the presence of the same disorder in a relative. Alternatively, the experience of having a psychiatric disorder may reduce the reluctance an individual feels in reporting the presence of a psychiatric disorder in a relative. It is also possible that experiencing a psychiatric disorder may have no direct effect on the reporting of psychiatric disorders in relatives; rather, the correlation between them might result from a third factor such as cooperativeness. That is, the observed pattern of results could be obtained if some individuals accurately reported the presence or absence of personal and family psychopathology, while other individuals consistently denied both even if they were present.

Even more importantly, our results do not address the crucial question of whether individuals with a history of a psychiatric disorder are more or less accurate informants about psychiatric illness in their relatives than are individuals who report no personal psychiatric history. In other words, do the higher rates of illness reported in relatives by affected informants derive mostly from false positives reported by affected informants or from false negatives reported by unaffected informants? Assume, for example, that a personal psychiatric history changes the threshold at which an individual recognizes psychiatric illness in his or her relatives. Do informants with no psychiatric disorder have their threshold set too high so that truly affected relatives are reported to be unaffected (false negatives) or do informants with a history of a psychiatric disorder have their thresholds set too low so that relatives with normal psychological reactions are reported as having a psychiatric disorder (false positives)?

Previous research in the family history method has generally concluded that false positives are considerably rarer than false negatives (1-6). We are in the process of interviewing the living and cooperative parents of this twin sample and hope in the future to be in a position to address this critical question definitively.

A final important research question is how an informant's psychiatric history influences family history diagnoses when they are based on information from several informants. It is possible that this technique, used frequently in modern family studies of psychiatric illness, may attenuate the impact of informants' psychiatric histories on the final family history diagnosis.

CONCLUSIONS

These results, if confirmed, have important implications for the use of family history information in psychiatric research and practice because they suggest that the psychiatric history of the informant must be consid-
er in interpreting the results of family history data. For example, one design for family history studies has been to compare the rates of a disorder in relatives of affected versus control probands by obtaining family history information from the affected and control probands, respectively. Our results suggest that positive findings in such a study may emerge because the disorder truly aggregates in families or because affected individuals more frequently report illness in their relatives than do unaffected individuals.

Before we can properly "correct" for the impact of a personal psychiatric history on family history reporting, however, further understanding of the nature of this impact is needed. For example, if unaffected informants do not recognize the presence of true psychiatric illness in relatives, might a more detailed characterization of the disorder at the time of the interview increase the level of recognition of the unaffected informant? If the problem results more from a hesitancy of unaffected informants to admit to psychiatric disorders in relatives, could techniques be used to reduce embarrassment, such as emphasizing the frequency of psychiatric disorders or allowing the relevant items to be self-administered? Regardless of the specific mechanism at work, our results suggest that the impact of an informant's psychiatric history on family history diagnoses is substantial and should be taken into account in interpreting results obtained by the family history method.

REFERENCES